REMARKS

Rejection of the claims under 35 USC 103:

Claims 5, 7, 8, and 21 have been rejected under 35 U.S.C. 103(a) as being anticipated by Adams et al. (US 2005/0153926) in view of Heller et al. (Journal of Applied Polymer Science, Vol. 22, p. 1991-2009, 1978).

Claims 12, 16, 17, and 22 have been rejected under 35 U.S.C. 103(a) as being anticipated by Adams et al. in view of Heller et al. and Tonge et al. (U.S. Patent 6,436,905).

Applicants respectfully disagree. It is the Applicants' opinion that knowledge of Adams et al., when combined with Heller et al., would not be reasonably expected to lead one to the polymers described and claimed in the instant application. The primary teaching of Adams et al. is a nucleic acid with an ethylene-containing moiety which can be covalently or non-covalently linked to a polymer (abstract) as a means of delivering the nucleic acid to a cell in vivo (background). In other words, the inventive concept of Adams et al. is an ethylene linked nucleic acid for use in incorporation into particles or substantially water-soluble polymers (last two sentences of paragraph [0011] and paragraph [0013]). In practice of the invention,

Adams et al. teach that: "The polymers of the invention can have substantially any structure achievable by using subunits having a polymerizable or otherwise reactive ethylene moiety." [0041] and "Examples of framework components suitable for use in the methods of the present invention include, but are not limited to, polymers, liposomes, micelles, colloids, biological particles and non-biological particles (e.g., silica beads, polymeric beads, gels, etc.). … It is understood that the present invention is intended to encompass all types of frameworks capable of presenting functional groups that are reactive towards the ethylene-containing moiety of the subunits." [0065].

Adams et al. teach that it is preferred that the subunits of the polymers are attached via cleavable moieties [0042]. A preferred cleavable moiety undergoes "cleavage due to a naturally occurring biological process" such that the polymer "is cleaved into smaller fragments by the acidic environment of the vacuole." [0045]. It is the Applicants' opinion that a stated desire for the polymer to be cleaved in an endosome does not provide motivation for a membrane active polyanion.

Adams et al. further teach that the hydrophobicity of the polymer "can be modulated by using a hydrophobic linking group" between the nucleic acid and the ethylene-containing moeity [0050-0052]. Thus, Adams et al. teach inserting a hydrophobic group between the nucleic acid and an ethylene-containing moiety. It is the Applicants' opinion that the insertion of a hydrophobic linking group between a nucleic acid and a polymer taught by Adams et al. would not be expected to motivate one skilled in the art of the desirability of a membrane active polyanion.

At paragraph [0057], Adams et al. teach that "the physicochemical characteristics (e.g., hydrophobicity, hydrophilicity, surface activity, conformation) of the polymer are altered by attaching a monovalent moiety which is different in composition than the constituents of the bulk polymer and which does not bear a nucleic acid." However, this description encompasses every conceivable modification without limit and does not teach or provide motivation for any particular desirable physicochemical characteristic. Further, Adams et al. teach attachment of a single monovalent moiety ("attaching a monovalent moiety'), and not a plurality of hydrophobic amines or alcohols as is claimed in the instant application.

Adams et al. teach, at paragraphs [0082]-[0084] that "exemplary copolymers include… styrene-maleic anhydride." And that "Other exemplary polymeric framework components include poly(maleic anhydride-co-vinyl ether)… poly(styrene-maleic anhydride)… ." However, it is readily known by those skilled in the art that these classes of polymers encompass polymers with a wide range of physicochemical characteristics and that not all poly(maleic anhydride-co-vinyl ether) and poly(styrene-maleic anhydride) polymers are membrane active. Applicants' claims do not encompass any and all poly(maleic anhydride-co-vinyl ether) polymers or poly(styrene-maleic anhydride) polymers, but are limited to a specific subset of polymers with a very specific physicochemical characteristic that is readily determined: capability of lysing mammalian cell membranes at pH 6.5.

For endosomal membrane disruption, Adams et al. teach only the usefulness of polycations. At paragraph [0136], Adams et al. teach "where it is desired to transfer nucleic acid molecules to target cells by injecting them intramuscularly to evoke an immune response, it will be found that this transfer can be effected by use of a multifunctional molecular complex of the present invention, as defined above, comprising a cationic polyamine to which is

attached, as the endosome membrane disruption promoting component, a lipophilic long chain alkyl group as defined above." At paragraph [0146], Adams et al. teach "The ability of poly-lysine to facilitate DNA entry into cells is significantly enhanced if the poly-lysine is chemically modified with hydrophobic appendages; (*ref*) complexed with cationic lipids; (*ref*) or associated with viruses." At paragraph [0148], Adams et al. teach the desirability of attaching fusogenic peptide to poly-lysine. Polyamines and poly-lysine are well known in the art to be polycations. It is further well known in the art that polycation readily associate, via electrostatic interaction, with nucleic acids and cell membranes, both of with a negatively charged. Adams et al. provide no suggestion that a polyanion could serve as a suitable substitute in these circumstances.

The Action states that the polymers taught by Adams et al. meet the structural limitations of the claims. It is the Applicants' opinion that this statement is true only in sense that the styrene-maleic anhydride random copolymers and ether-maleic anhydride alternating copolymer polymers described by Adams et al. encompass any and all physicochemical characteristics. Thus, because Adams et al. essentially teach any and all polymers without providing suggestion or motivation for modified styrene-maleic anhydride random copolymers and ether-maleic anhydride alternating copolymers capable of lysing mammalian cell membranes at pH 6.5, or any membrane active polyanion, one would not have been motivated to combine the synthetic method taught by Heller et al. to generate the Applicants' claimed membrane active polymers and method.

In light of their remarks, Applicants request reconsideration of the rejections.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 5, 7, 8, 12, 16-17 and 21-22 should be allowable.

Respectfully submitted,

/Kirk Ekena/

Kirk Ekena Reg. No. 56,672
Roche Madison Inc.
505 South Rosa Road
Madison, WI 53719
608-238-4400

I hereby certify that this correspondence is being transmitted to the USPTO on this date: 01/07/2009 .

/Kirk Ekena/
Kirk Ekena